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p-tert-Butyl thiacalix[4]arenes functionalized at the lower rim by *o*-, *m*-, *p*-amido and *o*-, *m*-, *p*-(amidomethyl)pyridine fragments as receptors for α-hydroxy- and dicarboxylic acids

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ABSTRACT

A series of new *p-tert*-butyl thiacalix[4]arenes with *o*-, *m*-, *p*-amido and *o*-, *m*-, *p*-(amidomethyl)pyridine substituents at the lower rim in *cone*, *partial cone*, and 1,3-*alternate* conformations were synthesized. The ability of the obtained compounds to recognize the α-hydroxy (glycolic, tartaric) and dicarboxylic (oxalic, malonic, succinic, fumaric, and maleic) acids was investigated by UV–vis spectroscopy. Also, the efficiency and selectivity of binding, the association constants log K_a (10^2 to 10^7 M^{-1}) and the stoichiometry were determined for the complexes of *p-tert*-butyl thiacalix[4]arenes with the acids. The receptors based on *p-tert*-butyl thiacalix[4]arenes with (amidomethyl)pyridine substitutes are most efficient in complexation in many cases.

1. Introduction

The principles for constructing the receptor molecules are based on careful studies of biological systems.[1] The creation of biomimetic receptor structures offers new opportunities for modeling artificial living systems and physiological processes,[2] therapeutic agents,[3] and sensors for medicine technology.[4,5] Biologically active compounds, among them carboxylic acids, are one of the most attractive targets in this field[6] because of their central role in many enzyme activities, DNA regulation, hormone transporting, peptide synthesis, and intracellular communication.[7,8] In addition, carboxylic acid groups are typically presented in the structure of many natural biomacromolecules, e.g., proteins.

Intensive development in this area led to the creation of a number of 'host' molecules for carboxylic acids, which are functionalized with various groups, i.e., calixarenes, porphyrins, cyclodextrins, and metal based systems.[9–18] Despite these achievements, a general approach for the receptor design for carboxylic acids has not been specified.[19–21]

Presently, one of the basic directions for selective binding of a protein surface involves recognition of amino and carboxylic groups of amino acid residues that prevail on the protein surface by means of a synthetic molecular platform.[14,16,22,23] For this purpose, rather simple and synthetically available molecules able to reversibly change various functions of proteins are demanded to create medical drugs and diagnostic tools.

Effective binding of acid side chains by receptors is extremely important for molecular recognition of α-hydroxylic and dicarboxylic acids.[20] In addition, the binding area between the receptor and substrate should be maximal.[20] This occurs if the receptor provides multiple interactions with a guest.[21]

Among other currently used artificial molecules, *p-tert*-butyl thiacalixarenes seem promising for these requirements.[20,21] Their three-dimensional structures with various sizes of internal cavity, number and type of binding centers, and spatial arrangement of binding groups are very applicable for the design of large number of receptors for highly selective recognition of the required substrates.[24] The thiacalixarene scaffold because of its pre-organization, easy one-pot preparation, and simple derivatization can be used as a building block for creation of the receptor molecules with various groups and different conformations (*cone*, *partial cone*, 1,2-*alternate*, and 1,3-*alternate*).

Presently, *p-tert*-butyl thiacalix[4]arenes are widely used as molecular platforms for the efficient recognition of anions and cations.[24–26] The modification of macrocyclic platforms provides new synthetic receptors for various substrates. Previously, several

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